WS16.1 Treatment of early diagnosed CFRD with oral drugs versus insulin: An open prospective randomized study

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Objective: CFRD is the most frequent comorbidity in CF. One reason for the recommendation to use Insulin as first line treatment is the lack of data supporting the use of oral anti-diabetic drugs. Nevertheless around 10% of all patients with CFRD are treated with oral drugs.
Method: We initiated a multi-centres trail (NCT 00662714), enrolling patients identified by screening for CFRD. In the study the effects of 3 daily insulin injections were compared to oral treatment with Repaglinide in a RCT over two years. The primary outcome parameter was HbA_1c as a marker of glycaemic control. Secondary outcome parameters were change in pulmonary function (FEV_1%pred) and change in BMI-Z-score.
73 patients with newly diagnosed CFRD were randomised. Age (mean±SD) 22.2±8.8 years, BMI-Z-score –0.74±1.1; HbA_1c 6.5±0.8%; FEV_1 66.9±23.5%pred.

Treatment effects after 1 and 2 years

Year	Treatment	Delta HbA1c (mean±SD)	FEV1%pred. (mean±SD)	BMI-Z-score (mean±SD)
1	Repaglidine	0.19±0.64	–2.7±8.6	–0.15±0.36*
	Insulin	–0.10±1.23	–1.7±10.8	0.12±0.44
2	Repaglidine	0.16±0.74	–3.2±6.1	–0.21±0.59
	Insulin	–0.24±1.32	–3.2±10.4	0.002±0.42

*$p < 0.05$ repaglinide vs Insulin.

After 1 year of treatment, BMI-Z-score was better with insulin but this did not persist after two years. There was no inferiority of the oral treatment in neither the primary nor the secondary outcome parameter after two years of treatment.
Conclusion: In this group of newly diagnosed patients with CFRD, the oral treatment with Repaglinide was a safe and effective therapeutic option. This is important because in this age group there are many challenges (e.g. start with a job) and the additional burden of insulin treatment might be postponed for at least two years.
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WS16.2 Glucose handling in CF – Implications for the diagnosis and screening of CFRD

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Introduction: The OGTT, based on the WHO criteria, is the recommended diagnostic test to screen for diabetes in CF. However the glucose response through the day has not been evaluated in CF subjects, who have a 'normal' standard OGTT. To study this further, we compared the diurnal response to a glucose a load in 13 pancreatic insufficient CF subjects with 10 healthy (age, BMI matched) controls.
Method: Subjects underwent a standard validated mixed meal test (75g CHO) at 0800, 1300 and 1800 hours on the same day. Blood glucose levels were measured over 120 minutes for each test meal. The area under the curve was calculated for the initial 30 (AUC_{30}) and total 120 (AUC_{120}) minutes of each test.
Results: See Table [Mean (SD)]. CF subjects had significantly higher AUC_{30} (morning and evening) and AUC_{120} (all times in the day) compared to controls. Although there was some diminution in glucose levels in CF patients during the afternoon, they increased again later in the day which was not seen in control subjects.
Conclusions: CF subjects have higher glucose levels not only in the morning but throughout the day. This has important clinical implications for the diagnosis of CFRD as more physiological tests that capture this effect should be used when assessing the glycaemic status CF patients.

Table. Diurnal glucose handling

	0800 h		1300 h		1800 h	
	AUC_{30}	AUC_{120}	AUC_{30}	AUC_{120}	AUC_{30}	AUC_{120}
Controls	151±29	564±120	155±17	605±69	160±21	638±101
CF	182±24	779±118	163±21*	638±85$^{\Delta}$	181±16$^{\Omega}$	806±132^

Within group: vs morning: *p = 0.004, $^{\Delta}$p = 0.0009; vs afternoon: $^{\Omega}$p = 0.03, ^p = 0.003.

Reference(s)

[1] Jarrett, R. BMJ 1972; 1(5794): 199–201.

WS16.3 Vitamin D supplementation in patients with cystic fibrosis: A pilot randomized controlled trial

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Objectives: Vitamin D (vit D) insufficiency is frequent in CF patients. Evidence of benefit of vit D in CF is weak. The effect of vit D on calcium homeostasis, inflammation, lung function and quality of life in CF patients was investigated in a pilot trial (ClinicalTrials.gov:NCT01321905).
Methods: Patients (16) were randomized to vit D2 or vit D3 or to serve as controls. The initial weekly dose of 35000/50000 IU (children/adults) was individually adjusted by monitoring s25OHD. Three months of intervention were followed by two of wash-out.
Results: S25OHD correlated with total vit D dose/kg BW, and with sun exposure. Patients on vit D3 had a transitory increase in albumin-corrected calcium at 1-week visit and higher s25OHD compared with controls at 3-months visit. In this group, serum IgA increased, eosinophils decreased and there was a tendency for decrease in IL-6 and CRP. Patients receiving vit D2 downregulated serum total IgG and upregulated lymphocytes. Patients reaching s25OHD 111–129 nmol/l increased their PEF, FEF25% and CFQ-R self-reported scores in the Emotion, Body, Weight and Respiratory domains. The CFQ-R parent-reported score for the Respiratory domain was higher in children reaching s25OHD 92–97 nmol/L compared with those reaching s25OHD 58–82 nmol/l. Accordingly, s25OHD correlated positively with FEV%, FEF50%, FEF75%, and CFQ-R scores for the Emotion and Respiratory domains. No vit D toxicity was seen.
Conclusion: Our results suggest that vit D supplementation in CF patients is safe and beneficial. Its effect may be clinically relevant when s25OHD is increased to 111–129 nmol/L, with positive impact on inflammation, lung function and quality of life.

WS16.4 Treatment algorithm for vitamin D deficiency – A review a year on

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Introduction: Fat soluble vitamins are poorly absorbed in CF, even in those with adequate pancreatic enzyme replacement, such that most patients have low serum levels and require supplementation. This is particularly important with vitamin D, where low levels are associated with poor bone mineralisation. However the correct amount of supplementation can vary, so to overcome this we developed and published a treatment algorithm (ECFC 2012). We wished to assess the efficacy of this tool in correcting vitamin D levels in our large adult CF clinic.
Method: We checked vitamin 25OHD levels pre and post treatment, following the introduction of the algorithm.
Results: See the table.

Vitamin 25OHD Levels pre and post treatment

Treatment Regime	Treatment period (months), Mean (range)	25OHD Levels (nmol/l), mean (range)		P value
		pre treatment	post treatment	
50,000iu Cholecalciferol weekly for 8 wks, 26 pts	5 (1–12)	17.6 (5.8–28.6)	78.6 (9.9–177.7)	<0.0001
Calcichew D3 forte b.d., 32 pts	6 (1–12)	37.7 (20.8–51.5)	57.3 (18.5–100.9)	<0.0001

Conclusion: We have shown that the use of our treatment algorithm has significantly improved vitamin D levels in patients with insufficient or deficient vitamin D status. Our aim is to continue with this approach to ensure that vitamin D levels are maintained above 50 nmol/l throughout the patients' lifetime.